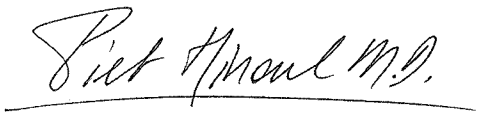
EXHIBIT 6

Clinical Expert Report

Gynecare PROLIFT +M™ Pelvic Floor Repair System



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September 25, 2012
Date

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A. MANUFACTURER'S STATEMENT ON THE CLINICAL DATA USED TO AFFIX CE-MARK:

The following clinical evaluation is based on the assessment of the risks and the benefits, associated with use of the device through:

- A compilation of relevant scientific literature that is currently available on Gynecare PROLIFT +M™ Pelvic Floor Repair System.
- The compilation of published literature includes publications from 2005 and the complaint analysis consists of data generated since the last submission in 2008.
- A review of the outcomes reported after GYNECARE PROLIFT™ Pelvic Floor Repair System in the scientific literature; as GYNECARE PROLIFT™ uses the same procedural technique to treat pelvic organ prolapse via the transvaginal approach.
- An analysis of expected adverse events based on MAUDE data, as well as relevant analysis of the published literature on complications following transvaginal pelvic organ prolapse repair kit procedures.

B. OBJECTIVE OF CLINICAL EVALUATION REPORT:

This Clinical Evaluation Report (CER) is an update of the CER dated 2/5/2008, and contains additional material that was not included in the prior version.

The purpose of this report is determine whether additional knowledge has become available pertinent to recognized or emerging hazards and whether the acceptability of these risks, should any be identified, change the benefit-risk profile of the device. The purpose of the report is also to assess whether the device continues to meet state of the art by performing safely and as intended and meeting its claims.

C. DEVICE DESCRIPTION & BACKGROUND:

BACKGROUND:

Synthetic materials have been used to reinforce the deficiencies in native tissue in the treatment of inguinal and incisional hernia defects and pelvic organ prolapse. Reinforcement materials were first widely used in hernia repair and the understanding of their use there has been applied to pelvic organ prolapse repair. In a review paper, Huebner and colleagues in 2006 described the challenges associated with the increased use of surgical mesh in pelvic floor surgery. The selection of a synthetic mesh for pelvic floor repair includes consideration of many characteristics including composition and architecture; these factors influence properties including strength, flexibility, and pore size. Among currently used synthetic meshes, most are in the Amid Classification of Type I, macroporous mesh with a pore size > 75µm. These mesh implants are typically constructed from monofilament polypropylene fibers.

Knitted, polypropylene mesh as a reinforcement for Hernia Repair has been used for 40+ years and is an accepted method for reducing recurrence of abdominal wall defects seen in both incisional and inguinal hernias. However, implantation of polypropylene mesh is associated with an increase in problems associated with the foreign material implant. Complications associated with these materials have led to changes in implant materials and construction with a goal to 1) reduce implant mass and 2) increase the mesh pore size (Klosterhalfen et al. 1998). The impact of such reductions in material mass on the durability of the repair must be considered. Assessing the breaking strength of healthy tissue, in vivo measurements of maximum pressure during the stresses of coughing, jumping and Valsalva maneuver, and mathematical modeling of abdominal wall forces, have led to the conclusion that synthetic mesh implants, even the lower mass mesh implants, are significantly stronger than required (Deprest et 2006, Cobb et al. 2005)). For further evidence, Cobb studied the burst strength of three mesh types (MARLEX Mesh, PROLENE Soft Mesh, and ULTRAPRO Mesh) in a porcine hernia model. Testing burst strength five months after implantation demonstrated that even the lowest mass mesh (ULTRAPRO Mesh) exceeded by 2X the estimated burst strength of native abdominal wall fascia burst strength. While providing what he felt was sufficient strength, he noted increased abdominal wall compliance with the lightweight mesh (ULTRAPRO Mesh) when compared to heavyweight mesh. He attributes this improvement to the reduced mass and the larger pore size of the lightweight mesh.

The table below describes material properties of several synthetic mesh implants of different construction and material density.

Table 1 - Characteristics of Various mesh implants

MESH	Unit Weight (mg/cm2) permanent component	Burst Strength, psi	Maximum Pore Size, mm
PROLENE* Polypropylene Mesh	7.6	234	<1
GYNECARE GYNEMESH* PS Nonabsorbable (PROLENE* Soft Mesh)	4.5	116	2.5
MERSILENE* Polyester Fiber Mesh	3.3	83	<1
VYPRO Mesh	2.5	71 (pre-absorption 90)	4.5
VYPROII Mesh	3.5		3-4
ULTRAPRO* Partially Absorbable Mesh (GYNECARE GYNEMESH M* Mesh)	2.8	90 (pre-absorption 135)	5.0

Reduction of the mass and the increase in the pore size of the mesh implant foreign body are seen to alter the inflammatory response which in turn is likely to alter tissue ingrowth and the resulting properties of the reinforced tissue. As the mass of a mesh implant is reduced and the pore size is increased, the surface area exposed to the host is reduced, and the foreign body reaction to the implant is reduced.

An example of this move towards lowering the mass of implanted mesh is seen in the work of a team of French surgical gynecologists (group TVM) that developed the procedure and mesh implant shape that became the GYNECARE PROLIFT System. During the initial development of the system the group used PROLENE Mesh as the implant in over 100 procedures. When GYNECARE GYNEMESH PS became available, the team readily switched to that implant material in an attempt to address two concerns they observed in the earliest cases; erosion of the mesh through the vaginal wall and tissue contraction leading to stiffening and distortion of the vaginal wall. When the system was commercially released as the GYNECARE PROLIFT System, the implant was GYNECARE GYNEMESH PS Mesh. As shown in Table 1, by using GYNECARE GYNEMESH PS instead of PROLENE Mesh for the same size implant, 1) the implant mass was reduced by almost 50%, 2) the pore size of the implanted mesh was also significantly increased with this change, and 3) the strength of the mesh was reduced. Although direct comparison of subjects treated with the different mesh implants is not possible, as many other changes in the technique were occurring in parallel to the mesh implant change, in practice, the group did prefer the lower mass of the GYNECARE GYNEMESH PS and observed no change in repair effectiveness.

Although further reduction in the mass of the implanted mesh below that of GYNECARE GYNEMESH PS Mesh can be justified based on strength requirements, the handling of such a lightweight mesh during insertion can be challenging. A minimum stiffness along with the ability to maintain shape is necessary to ease placement of the implant. By adding absorbable filaments to a lightweight polypropylene mesh construct, an implant can be produced that provides acceptable handling characteristics during implantation while meeting the goal of reducing the ultimate implant mass.

Design Changes

With these considerations, the modification to the GYNECARE PROLIFT System was undertaken. The proposed change to the system, from the GYNECARE PROLIFT System to the GYNECARE PROLIFT+M, as described previously, involves modifying only the mesh components of the system and the packaging of that component. The indications for use and the training are essentially unchanged. The new mesh, GYNECARE GYNEMESH M, is a pre-shaped partially absorbable mesh based on ULTRAPRO Partially Absorbable Mesh developed by ETHICON, INC.

ULTRAPRO Mesh is currently indicated for tissue reinforcement and long lasting stabilization of fascial structures of the abdominal wall and used for hernia repair by general surgeons. The mesh includes monofilament polypropylene and fibers of polyglecaprone, the same material used in ETHICON MONOCRYL Monofilament Absorbable Suture. Animal testing of both the polypropylene substrate and the final mesh adding the polyglecaprone fibers in a rat model showed that the inclusion of the absorbable filaments introduced no short-term complications and no negative impact on biocompatability. Using a rodent model, the authors evaluated both materials after 28, 56, and 84 days of implantation. They reported a slight inflammatory tissue reaction near the mesh filaments involving macrophages and foreign body giant cells. Initial degradation of the absorbable component (in the composite mesh) was noted at 56 days, and all material was absorbed by the 84-day observation period. Although this absorbable material had not previously been used in the construction of a surgical mesh, it has a long history of implantation as MONOCRYL Suture. The authors observed no negative effects on the biocompatibility of PROLENE Mesh with the addition of the absorbable filaments and felt the composite mesh suitable for hernia repair.

The experience reported with mesh implants of varying unit weight (density), pore size, and burst strength indicates that the use of GYNECARE GYNEMESH M, based on ULTRAPRO Mesh, will provide the necessary strength to reinforce tissue and provide long lasting stabilization of the fascial structures in vaginal wall prolapse. GYNECARE GYNEMESH M has burst strength that exceeds two other mesh implants, MERSILENE Mesh and VYPRO Mesh that both have been successfully used for pelvic organ prolapse reported in the literature. GYNEMESH M is biocompatible and elicits minimal foreign body reaction as shown in internally conducted animal studies.

DESCRIPTION:

The GYNECARE PROLIFT+M™ Total, Anterior, and Posterior Pelvic Floor Repair Systems consist of pre-cut GYNECARE GYNEMESH M™ Mesh implants and a set of instruments to facilitate mesh implant placement.

The mesh implant is provided separate from the instruments, in a foil pouch with a paper folder designed for easy access of the mesh implant. The mesh implant may be trimmed while held in the paper folder.

The following table summarizes the instruments included with each system:

Table 1 – GYNECARE PROLIFT+M™ Pelvic Floor Repair System Components

Repair System	Components			
	Mesh Implant	Guide	Retrieval Devices	Cannula
Total	1 Total	1	6	6
Anterior	1 Anterior	1	4	4
Posterior	1 Posterior	1	2	2

GYNECARE GYNEMESH M™

GYNECARE GYNEMESH M™ Mesh is manufactured from approximately equal parts of absorbable poliglecaprone-25 monofilament fiber and non-absorbable polypropylene monofilament fiber. The polymer of the undyed and dyed polypropylene fiber (phthalocyanineblue, Color Index No.: 74160) is identical to the material used for dyed / undyed PROLENE® Polypropylene Suture material. Blue PROLENE® Suture monofilaments have been incorporated to produce contrast striping in the mesh. Poliglecaprone-25 fiber consists of a copolymer containing glycolide and ε-caprolactone; this copolymer is identical to the material used for MONOCRYL® (Poliglecaprone 25) Suture. The absorbable poliglecaprone part of the mesh aids handling, making intraoperative manipulation and positioning of the mesh easier. After absorption of the poliglecaprone- 25 component, only the polypropylene mesh remains, which has burst strength of approximately 621 kPa (90 psi).

Total Implant

The Total Implant is constructed from GYNECARE GYNEMESH M™ Mesh and is shaped for performing a total vaginal repair. The Total Implant has six straps: four for securing the anterior portion of the implant via a transobturator approach and two for securing the posterior portion of the implant in the sacrospinous ligament via a transgluteal approach. Alternatively, the two posterior straps may be cut to reduce their length and secured in the sacrospinous ligament via a vaginal approach. The proximal and distal anterior straps have squared and triangular ends, respectively, while the posterior straps have rounded ends (see Figure 1a).

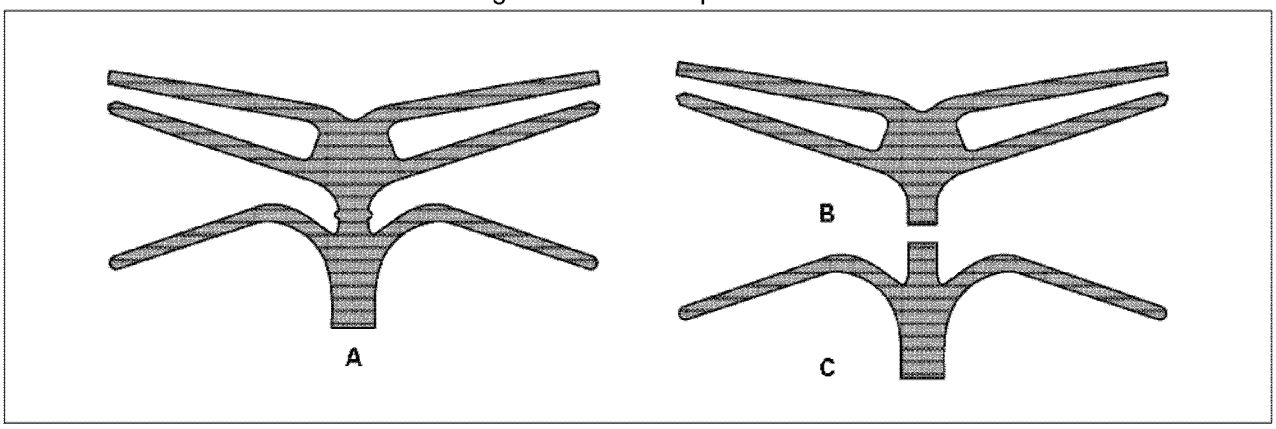
Anterior Implant

The Anterior Implant is constructed from GYNECARE GYNEMESH M™ Mesh and is shaped for repair of anterior vaginal defects. The Anterior Implant has four straps that are secured via a transobturator approach. The proximal and distal anterior straps have squared and triangular ends, respectively (see Figure 1b).

Posterior Implant

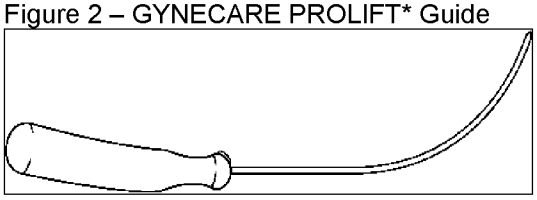
The Posterior Implant is constructed from GYNECARE GYNEMESH M™ Mesh and is shaped for repair of posterior and/or apical vaginal vault defects. The Posterior Implant has two straps that are secured in the sacrospinous ligament via a transgluteal approach. Alternatively, the two posterior straps may be cut to reduce their length and secured in the sacrospinous ligament via a vaginal approach. The posterior straps have rounded ends (see Figure 1c).

Figure 1 – Mesh Implants



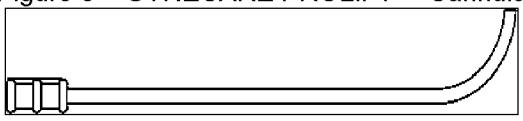
The GYNECARE PROLIFT* Guide is a single-patient-use instrument designed to create tissue paths to allow placement of the Total, Anterior, and Posterior mesh implants and to facilitate placement of the GYNECARE PROLIFT Cannula. Its length and curvature are specifically designed to create proper placement paths for all mesh implant straps. The GYNECARE PROLIFT Guide is suitable for use on both sides of the patient (see Figure 2).

Figure 2 – GYNECARE PROLIFT* Guide



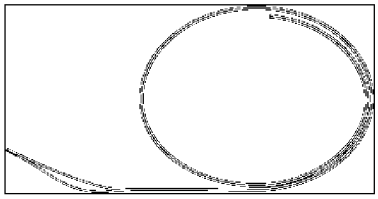
The GYNECARE PROLIFT* Cannula is a single-patient-use instrument used in conjunction with the GYNECARE PROLIFT Guide to facilitate passage of the implant straps while protecting the surrounding tissue. Each GYNECARE PROLIFT Cannula is placed over the GYNECARE PROLIFT Guide prior to passage and remains in place after the GYNECARE PROLIFT Guide is withdrawn (see Figure 3).

Figure 3 – GYNECARE PROLIFT™ Cannula



The GYNECARE PROLIFT* Retrieval Device is a single-patient-use instrument designed to facilitate placement of the mesh implant straps. The GYNECARE PROLIFT Retrieval Device is passed through the previously positioned GYNECARE PROLIFT Cannula until its distal end is retrieved through the vaginal dissection. The distal end of the GYNECARE PROLIFT Retrieval Device has a loop to securely capture the mesh implant strap as the strap is drawn out through the GYNECARE PROLIFT Cannula *(see Figure 4).*

Figure 4 – GYNECARE PROLIFT™ Retrieval Device



PERFORMANCE

Animal studies show that implantation of GYNECARE GYNEMESH M™ Mesh elicits a minimum to mild inflammatory reaction which is followed by collagen tissue ingrowth through the mesh, thus incorporating the mesh into adjacent tissue. The mesh remains soft and pliable, and normal wound healing is not noticeably impaired.

In GYNECARE GYNEMESH M™ Mesh implanted subcutaneously in rats, the poliglecaprone-25 copolymer is essentially absorbed within 84 days after implantation. The polypropylene portion is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes. In an animal model, excessive connective tissue deposition and deleterious scar plate formation did not occur. The mesh construction permits trimming of the implant without unraveling.

STERILITY

The GYNECARE PROLIFT+M™ Systems are sterilized by ethylene oxide. DO NOT RESTERILIZE. DO NOT REUSE. Reuse of this device (or portions of this device) may create a risk of product degradation and crosscontamination,
which may lead to infection or transmission of bloodborne pathogens to patients and users. Do not use if package is opened or damaged. Discard all opened, unused devices.

DISPOSAL

Dispose of the devices and packaging according to your facility's policies and procedures concerning biohazardous materials and waste.

STORAGE

Recommended storage conditions: controlled room temperature and relative humidity (approximately 25°C, 60% RH), away from moisture and direct heat. Do not use after expiry date.

INDICATIONS

The GYNECARE PROLIFT+M™ Total, Anterior, and Posterior Pelvic Floor Repair Systems, through placement of GYNECARE GYNEMESH M™ Partially Absorbable Mesh, are indicated for tissue reinforcement and long
lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment is intended, either as mechanical support or bridging material for the fascial defect.

CONTRAINDICATIONS

• GYNECARE GYNEMESH M™ Mesh should not be used in infants, children, pregnant women, or women planning future pregnancies, as the mesh will not stretch significantly as the
patient grows.
• GYNECARE GYNEMESH M™ Mesh must always be separated from the abdominal cavity by peritoneum.
• GYNECARE GYNEMESH M™ Mesh must not be used following planned intra-operative or accidental opening of the gastrointestinal tract. Use in these cases may result in contamination of

the mesh, which may lead to infection that may require removal of the mesh.
• The GYNECARE PROLIFT+M™ Systems should not be used in the presence of active or latent infections or cancers of the vagina, cervix, or uterus.

WARNINGS
• Patients on anticoagulation agents undergoing surgery using the GYNECARE PROLIFT+M™ System must have their anticoagulation therapy carefully managed.
• Do not remove the GYNECARE PROLIFT™ Cannulas from the patient until the mesh implant has been properly positioned.
• A digital rectal exam should be performed to detect possible rectal perforation.
• Cystoscopy may be performed to confirm bladder integrity or detect possible bladder or ureteral perforation.
• Post-operatively the patient should be advised to refrain from intercourse, heavy lifting and/or exercise (e.g. cycling, jogging) until the physician determines when it is suitable for the patient to return to her normal activities.
• Use the GYNECARE PROLIFT+M™ Systems with care, and with attention to patient anatomy and to proper dissection technique, to avoid damage to vessels, nerves, bladder, bowel, and vaginal wall perforation. Correct use of the GYNECARE PROLIFT+M™ Systems components will minimize risks.
• Transient leg pain may occur and can usually be managed with mild analgesics.

PRECAUTIONS
• Users should be familiar with surgical procedures and techniques involving pelvic floor repair and synthetic meshes before employing the GYNECARE PROLIFT+M™ Systems.
• Avoid placing excessive tension on the mesh implant during placement.
• Do not manipulate the GYNECARE PROLIFT™ Retrieval Device with sharp instruments or cut it to alter its length.
• Do not affix the GYNECARE GYNEMESH M™ Mesh Implant with any staples, clips, or clamps as mechanical damage to the mesh may occur.
• This product should only be used under the prescription of a physician.
• In patients with compromised immune systems or other conditions that would compromise healing the risks and benefits should be carefully weighed.
• Vaginal or urinary tract infection should be treated and alleviated prior to implantation.
• Acceptable surgical practice should be followed for the GYNECARE PROLIFT+M™ Systems as well as for the management of infected or contaminated wounds. If the Mesh Implant is used in contaminated areas it must only be with the understanding that subsequent infection may require its removal.
• Prolapse repair may unmask pre-existing incontinence conditions.
• Prophylactic antibiotics can be administered according to the surgeon's usual practice.
• The use of this product with tissue adhesives is not recommended, as data are not currently available.

ADVERSE REACTIONS
• Potential adverse reactions are those typically associated with surgery employing implantable materials of this type, including hematoma, urinary incontinence, urinary retention/obstruction, ureter obstruction, voiding dysfunction, pain, infection potentiation, wound dehiscence, nerve damage, recurrent prolapse, inflammation, adhesion formation, fistula formation, contracture, scarring, and mesh exposure, erosion, or extrusion.
• Punctures or lacerations of vessels, nerves, bladder, urethra or bowel may occur during GYNECARE PROLIFT™ Guide passage and may require surgical repair.
• Potential adverse reactions are those typically associated with pelvic organ prolapse repair procedures, including pelv

LITERATURE REVIEW

Search strategy literature review:

Examine literature from 1/1/2005 (First pelvic floor mesh repair kit launched in 2005: Prolift™ Pelvic Floor Re[pair System) to 9/1/2012.

Comprehensive article gathering, by including all relevant terms: "Prolift +M" and "Resorbable, Mesh, Prolapse" and hand searching following a general search on mesh and prolapse.

Search Databases

- Cochrane Review
- Google Scholar
- Medline
- NICE
- PubMed
- Scopus

Summary Findings & Selection Criteria

- 6 articles pertinent to Prolift+M™, in total, were identified
  - 4 reporting on prospective data (Level of Evidence: 2a)
  - 2 publications specific to the biomechanical and histological data specifically related to the partially resorbable mesh used in Prolift+M (Level of Evidence: Pre-clinical)
- Note: Results per search term:
  - Prolift+M:, following a hand search of related articles 4 more articles were identified and included.
  - Resorbable Mesh Prolapse: yielded 31 articles in this time period but most relate to meshes involving Polyglactin or Biological meshes that cannot be compared to Polyglecaprone.
  - Prolift: 92
    - 27 articles were identified to report both on success rates and adverse events with a minimum follow up of 6 months in the English literature and published in a PubMed cited journal in the period 1/2005-3/2012. This meta-analysis performed in 4/2012 is used in this CER as it represents the most studied pelvic floor mesh kit to date. The peroperative morbidity may not correspond entirely as the Prosima kit does not involve deep passes using trochars but the mesh implant and long term morbidity associated with the mesh is deemed to be an appropriate comparator.
  - The results from the Prolift literature review is covered in the risk benefit analysis.

The abstracts of these articles are summarized below:

- *Milani AL, Hinoul P, Gauld JM, Sikirica V, van Drie D, Cosson M; Prolift+M Investigators. Trocar-guided mesh repair of vaginal prolapse using partially absorbable mesh: 1 year outcomes. Am J Obstet Gynecol. 2011 Jan;204(1):74.e1-8.*

OBJECTIVE: To evaluate anatomic and functional outcomes at 1-year following trocar-guided transvaginal prolapse repair using a partially absorbable mesh.
STUDY DESIGN: Prospective multicentre cohort study at 11 international sites. One hundred twenty-seven patients with pelvic organ prolapse stage ≥ III had surgery and were evaluated at 3 months and 1-year postsurgery compared with baseline. Instruments of measurements: Pelvic Organ Prolapse Quantification, Pelvic Floor Distress Inventory-20, Pelvic Floor Impact Questionnaire-7, Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire-12, and Patients Global Impression of Change.
RESULTS: Anatomic success, defined as prolapse stage ≤ I in the treated vaginal compartments, was 77.4% (95% confidence interval, 69.0-84.4%). Significant improvements in bother, quality of life, and sexual function were detected at 3 months and 1 year compared with baseline. At 1-year after surgery, 86.2% of patients

indicated their prolapse situation to be "much better." Mesh exposure rate was 10.2% and rate of de novo dyspareunia 2% at 1 year.
CONCLUSION: These results demonstrate improved anatomic support, associated with excellent functional improvements, without apparent safety concerns.

- *V. Lucente, P. Hinoul, J. Gauld, P Jones, S. Khandwala, D Van Drie, M. Cosson, AL Milani. Medium term clinical outcomes following trocar guided mesh repair of vaginal prolapse using partially absorbable mesh. (Abstracts IUGA 2012 and AUGS 2012 Annual Meeting)*

Objectives: To evaluate anatomic and functional outcomes at 3 years following trocar-guided transvaginal prolapse repair using a partially absorbable mesh.
Methods: Prospective multicentre cohort study at 11 international sites. 128 patients with Pelvic Organ Prolapse Quantification (POP-Q) Stage≥ III were included. Concurrent hysterectomies and/or perineal repairs were allowed; exclusion criteria included other additional surgical repair of prolapse and previous prolapse repair using mesh. Patients underwent transvaginal mesh placement (Gynecare Prolift+M Pelvic Floor Repair System, Ethicon, Somerville, NJ). Evaluations were at 3 months, 1, 2 and 3 years post-surgery. The primary outcome measure was defined as anatomic success, POP-Q Stage 0-I, in the treated compartment. Patients requiring re-intervention for prolapse in the treated compartment were considered failures. Secondary outcome measures included an alternative anatomic measure defined as leading edge above the hymen (i.e. all POP-Q values less than 0 cm), Pelvic Floor Distress Inventory-20, Pelvic Floor Impact Questionnaire-7, Pelvic Organ Prolapse / Urinary Incontinence Sexual Function Questionnaire-12, and Patients Global Impression of Change. Complications were recorded.
Results: Of the original 128 patients undergoing surgery, 109 (85%) provided 3 year follow up data. Anatomic success, defined as POP-Q stage ≤ I in the treated vaginal compartments, was 75.9% (95% CI 66.7 to 83.6%, Clopper-Pearson method). Leading vaginal edge above the hymen in the treated side was achieved in 88.0% (95% CI 80.3 to 93.4%) of patients. 6 patients required reintervention for recurrent prolapse in the treated compartment. Patient reported outcomes are summarized in Table 1. Pelvic symptoms and sexual function improved significantly from baseline ($p<0.01$). Mesh exposure was observed in 19 patients over 3 years (14.8%); 14 of which occurred within the first 12 months post surgery. 10 of 19 exposures were at the apex, the majority following a total repair, 14 required a partial mesh excision. 2 patients had ongoing mesh exposure at 3 years, being treated conservatively. Incidence of mesh exposure varied between sites (0-20%). At 3 years, no patients had de novo pelvic pain; 3 (2.8%) had pain when the mesh was palpated during pelvic examination. Resolution of pre-existing pelvic pain occurred in 7 (5.5%) patients. Similarly, de novo dyspareunia was observed in 3/33 patients (9%), while preexisting dyspareunia resolved in 6/18 (33%).
Conclusions: These medium term results indicate that this standardized transvaginal mesh repair with a partially resorbable mesh yields sustainable anatomic and functional results. No major safety concerns were identified, and the low incidence of pain and dyspareunia was encouraging.

Table:

		Baseline N=128	1 year N=125	2 years N=123	3 years N=109
PFDI-20		98.9 (52.0)	25.9 (28.0)*	28.8 (29.2)*	28.0 (33.5)*
PFIQ-7		74.5 (70.5)	9.5 (23.4)*	12.5 (30.3)*	9.5 (24.1)*
PISQ-12		33.4 (7.8); n=58	39.3 (4.1)*; n=54	39.1 (4.5)*; n=49	39.8 (4.2)*; n=38
PGI-C	Much better		86.6%	88.4%	89.8%
	A little better		9.2%	7.1%	7.1%
	About the same		2.5%	3.6%	3.1%
	A little worse		0.8%	0.9%	-
	Much worse		0.8%	-	-

Differences from baseline: probability values denoted as * for p<0.001. Data presented as mean (± SD) except for PGI-C which is reported as %. PFDI-20 and PFIQ-7 scores range from 0 (best score) to 300 (worst score); sub-scales score range from 0 (best score) to 100 (worst score). PISQ-12 scores range from 0 (worst score) to 48 (best score). PISQ-12 was only collected for patients who were sexually active (n=60). Missing data were excluded.

- *Khandwala S, Jayachandran C. Transvaginal mesh surgery for pelvic organ prolapse--Prolift+M: a prospective clinical trial. Int Urogynecol J. 2011 Nov;22(11):1405-11*

INTRODUCTION AND HYPOTHESIS: This study deals with assessment of safety, efficacy, and potential complications of Prolift+M system to correct uterovaginal prolapse.
METHODS: We analyzed a prospective cohort treated with the Gynecare PROLIFT+M mesh system between October 2008 and March 2010. A composite score that included subjective/objective cure and lack of complications was used to assess treatment success.
RESULTS: One hundred sixty-seven women (age 65.1 ± 11.2 years, BMI 29.2 ± 5.8 kg/m(2)) were treated for pelvic organ prolapse using the PROLIFT+M system. Seven anterior Prolift+M, 42 posterior Prolift+M, and 118 total Prolift+M mesh surgeries were performed in patients with stage II or greater degrees of prolapse. Mean operative time was 122.7 ± 43.9 min. Mean intraoperative blood loss was 119.4 ± 125.3 ml. Our composite success score was 72.5% (treatment failures per POP-Q stage 1.4%, perception of bulge 4.4%, erosions 3.6%, pain/dyspareunia 3.7%, incontinence 0.7%, de novo urge urinary incontinence 8.7%, voiding dysfunction 0.6%, recurrent urinary tract infection 2.2%, and anal incontinence 2.2%).
CONCLUSIONS: Prolift+M surgery is safe and effective with minimal postoperative morbidities.

- *Roy S, Mohandas A, Coyne K, Gelhorn H, Gauld J, Sikirica V, Milani AL. Assessment of the psychometric properties of the Short-Form Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) following surgical placement of Prolift+M: a transvaginal partially absorbable mesh system for the treatment of pelvic organ prolapse. J Sex Med. 2012 Apr;9(4):1190-9. doi: 10.1111/j.1743-6109.2011.02640.x.*

INTRODUCTION: Impairment of sexual function is a significant problem among women suffering from pelvic organ prolapse (POP). Because anatomical measures of POP do not always correspond with patients' subjective reports of their condition, patient-reported outcome measures may provide additional valuable information regarding the experiences of women who have undergone surgery. The Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) is a validated, widely used condition-specific questionnaire focused on sexual function among patients with POP or urinary incontinence.
AIM: This study aims to report sexual function outcomes as measured by PISQ-12 and to evaluate the psychometric characteristics of the questionnaire following surgical mesh implant for the treatment of POP.
MAIN OUTCOME MEASURES: The PISQ-12 was used to measure sexual function, while a set of other measures, namely, Pelvic Organ Prolapse Quantification, Patient Global Impression of Change, Pelvic Floor Distress Inventory, Pelvic Floor Impact Questionnaire, and Surgical Satisfaction Questionnaire, was used for validation.
METHODS: Data for the study were collected from a prospective multicenter, single-arm study of surgical POP repair via the transvaginal placement of a partially absorbable mesh system. For baseline, month 3, and month 12 following POP surgery, several psychometric properties of the PISQ-12 were evaluated, including internal consistency (Cronbach's alpha), concurrent validity, discriminant validity, and responsiveness.
RESULTS: As measured by the PISQ-12 questionnaire, statistically significant improvements were observed in the composite summary score as well as all three subscale scores at 1 year. The PISQ-12 generally demonstrated good psychometric properties including internal consistency reliability, validity, and responsiveness. The PISQ-12 items had good distributional properties at baseline, with substantial ceiling effects at follow-up visits reflecting improvements experienced by the patients.
CONCLUSION: The PISQ-12 is a valid measure of sexual function in studies involving patients with POP.

- *Ozog Y, Konstantinovic M, Werbrouck E, De Ridder D, Mazza E, Deprest J. Persistence of polypropylene mesh anisotropy after implantation: an experimental study. BJOG. 2011 Sep;118(10):1180-5. doi: 10.1111/j.1471-0528.2011.03018.x. Am J Obstet Gynecol. 2011 Jan;204(1):74.e1-8.*

OBJECTIVE: To determine whether anisotropy persisted after incorporation into the host, using a standardised rabbit model for abdominal wall reconstruction. DESIGN: Investigator-initiated prospective-controlled experimental study. SETTING: Centre for Surgical Technologies, Medical Faculty KU-Leuven. SAMPLE: Fifteen New Zealand White rabbits. METHODS: In each rabbit, four full thickness primarily repaired abdominal wall defects were covered by a 4 × 5-cm Prolift+M implant (Johnson & Johnson, Norderstedt, Germany), either with the stiffest (n = 6 rabbits) or most elastic (n = 6) direction parallel to the body axis. Prolift+M contains 32 g/m² polypropylene, reinforced with polyglecaprone fibres. Harvesting was performed after 30, 60 and 120 days (n = 2 each time-point). The abdominal wall of three unoperated rabbits was used as negative control. MAIN OUTCOME MEASURES: Contraction, compliance and maximal strain and stress determined by uniaxial tensiometry. Results: Anisotropy properties persist at lower, more physiological displacements, but not at higher displacements. The stiffness of a mesh-augmented repair in the lower strain range remains above that of native tissue. Eventual mesh contraction was limited to 4.3%. Conclusions: Anisotropic properties of Prolift+M persist in vivo and shrinkage is minimal. Compliance of mesh-augmented repair remains less than that of native tissue. The functional consequences of this remain to be studied.

- *Ozog Y, Mazza E, De Ridder D, Deprest J. Biomechanical effects of polyglecaprone fibers in a polypropylene mesh after abdominal and rectovaginal implantation in a rabbit. Int Urogynecol J. 2012 Oct;23(10):1397-402.*

INTRODUCTION AND HYPOTHESIS: To investigate the biomechanical effects of polyglecaprone fibers in lightweight meshes implanted into the vaginal and abdominal wall of parous rabbits.
METHODS: New Zealand White rabbits (n = 24) were implanted with polypropylene meshes (32 g/m(2)), with (Prolift plus M, n = 12) or without (Prolift minus M, n = 12) polyglecaprone fibers. Following implantation in the posterior vaginal and abdominal wall, local side effects were evaluated and explants underwent uniaxial tensiometry after 120 and 180 days.
RESULTS: The vaginal extrusion rate was at least 50 %, coinciding with a minimum of 20 % of contraction. There were no measurable effects of the addition of polyglecaprone on tensiometric strength and compliance in abdominal explants.
CONCLUSIONS: The addition of polyglecaprone fibers did not compromise the biomechanical properties nor did it prevent vaginal extrusion and contraction. The latter as well as some other limitations preclude the rabbit vagina to be a suitable model for biomechanical testing.

D. LITERATURE REVIEW AND CLINICAL DATA – CONCLUSION STATEMENT:

The above data on Prolift +M™, taken together with the available data on Prolift™ and Ultrapro™ are sufficient to demonstrate compliance with the essential requirements covering safety and performance of PROLIFT+M™ under normal conditions of use. Clinical data collection over a medium term follow up was sponsored by the company and adequately reported upon.

E. COMPLAINT / ADVERSE EVENT REVIEW:

Tables 1-5 summarize the safety data as collected in the company sponsored trial: **Ethicon Sponsored Study; (Study # 300-07-006) A Prospective, Multi-center Study to Evaluate the Clinical Performance of the GYNECARE PROLIFT + M™ Pelvic Floor Repair System as a Device for Pelvic Organ Prolapse; (Clinicaltrials.gov identifier: NCT00833001)**. We believe this data provides the most in depth understanding of the safety profile of the Prolift+M™ device to date. The data (in part, as the three year manuscript has been reported upon at the IUGA and AUGS annual meeting, but the manuscript is still under preparation) correspond to the studies cited in the literature by Milani, et al. AJOG 2010.

Table 6 reviews the reported complaints to the company from launch to August 2012.

Table 7 summarizes complications registered in the MAUDE data base (1/2007 to 9/2012)

Table 1: Adverse events associated with GYNECARE PROLIFT +M™ repair

Adverse event		N patients experiencing (n=128)	Number of new events at each time period				
			6 months	12 months	24 months	36 months	Cumulative Events
Mesh exposure		19 (14.8%)	9	6	1	4	20
Mesh erosion		0	0	0	0	0	0
Pelvic pain[1]		8 (6.3%)	4	1	2	1	8
Infection	UTI	5 (3.9%)	4	1	0	0	5
	Wound	2 (1.6%)	2	0	0	0	2
	Other	2 (1.6%)	2	0	0	0	2
Dyspareunia (de novo)[2]		4 (3.1%)	0	1	0	3	4
Shortening[3]		2 (1.6%)	0	2	0	0	2
Scarring		1 (0.8%)	0	0	0	1[10]	1
Bleeding[4]		2 (1.6%)	2	0	0	0	2
Discharge[5]		0	0	0	0	0	0
Fistula		0	0	0	0	0	0
Temporary urine retention[6]		8 (0.6%)	9	1	0	0	10
DeNovo SUI[7]		14 (10.9%)	3		8	3	14
Bladder Perforation (n)		3 (2.3%)	3	0	0	0	3
Bowel Perforation (n)		0	0	0	0	0	0
Neuromuscular[8]		1 (0.8%)	1	0	0	0	1
Revision / resurgery	POP treated side	7 (5.5%)	2	1	2	2	7
	POP untreated side	6 (4.7%)	0	1	3	2	6
	Mesh exposure	15[9] (11.7%)	8	6[#]	0	2	16[#]
	Hemorrhage	0	0	0	0	0	0

[1] All AEs of “pelvic pain”, “vaginal pain”, “pelvic discomfort”. Not using data from Listing 16.2.7.1.11
[2] From listing 16.2.6.7.2
[3] From listings 16.2.6.7.1 if “yes” to: reduced vaginal capacity; vaginal tissue retraction / vaginal stenosis; introital stenosis and AE “shrinking of mesh” (pt 24005)
[4] AEs with MedDRA PT “Vaginal Haemorrhage” or “Haemorrhage” (pts 21004 & 28005)
[5] AEs with MedDRA PT “Vaginal Discharge”
[6] From Listing 16.2.7.1.3 – All AEs with MedDRA PT of “urinary retention” or “residual urine”.
[7] From PFDI Q17 & 18. Not necessarily reported as an AE
[8] Pt 12004 “Sciatica”
[9] 4 mesh excisions required hospitalisation
[10] Pt 24008 “small scar at vaginal vault” from re-intervention procedure
[#] Includes Pt 24013, withdrew consent at 12 months prior to planned mesh revision

Table 2 puts the data into perspective with existing published data on traditional repairs.

Table 2: Twelve-month adverse events associated with non-mesh repairs based on three IIS RCT'S compared to 12 month adverse events associated with GYNECARE PROLIFT+M™

		IIS Primary Investigators 12 month data for non-mesh repair					PROLIFT +M™ 12 months
		Carey	**Withagen**	**Altman**	**∑**	**%**	**n (%)**
Adverse events (at 12 months)							
Number of Patients (n)		70	97	189	356		128
Attended 12 mth FU		61	96	182	339	95.2	128
Pelvic pain		NR	10/85	1/182	11/267	4.1	5 (3.9%)[#]
De Novo Pain		NR	2/50	1/182	3/232	1.3	2 (1.6%)
Infection	UTI	NR	NR	9/189	9/189	4.8	5 (3.9%)
	Wound	NR	NR	0	0/182	0	2 (1.6%)
	Perineal	NR	NR	NR	NR	-	2 (1.6%)
Dyspareunia (total)		13/33	12/51	NR	25/84	29.8	5/66 (7.6%)
Dyspareunia (de novo)		5/12	3/29	NR	8/41	19.5	1/49 (2%)
Shortening		NR	NR	NR	NR	-	2 (1.6%)
Scarring		5	NR	NR	5/61	8.2	0
Bleeding		0	NR	1/182	1/243	0.4	2 (1.6%)
Discharge		NR	NR	NR	NR	-	0
Fistula		NR	NR	NR	NR	-	0
Temporary urine retention		NR	5/97	8/189	13/286	4.5	7 (5.5%)[*]
De Novo SUI		NR	8/88	11/176	19/264	7.2	17 (13.3%)[$]
Bladder perforation (n)		1/70	0/97	1/189	2/352	0.6	3 (2.3%)
Bowel perforation (n)		1	NR	NR	1/70	1.4	0
Neuromuscular		NR	NR	NR	NR	-	1 (0.8%)
Revision / resurgery	POP treated side (n)	2/61	4/96	1/182	7/339	2.1	3 (2.3%)
	Mesh exposure	0	0	0	0 (NA)	NA	15 (11.7%)
	Hemorrhage	NR	1	NR	1/97	1	0
	Vaginal stenosis	2	NR	NR	2/70	2.9	0

[#]:2 reported pain during routine activities, in 3 it was only elicited during pelvic examination.
[*]:reported as voiding dysfunction in Milani et al.
[$]:reported as both worsening and de novo SUI by Milani et al.

Sources Native Tissue Repair data:

- Carey M, Higgs P, Goh J, Lim J, Leong A, Krause H, Cornish A. Vaginal repair with mesh versus colporrhaphy for prolapse: a randomized controlled trial. BJOG. 2009 Sep;116(10):1380-6
- Withagen MI, Milani AL, den Boon J, Vervest HA, Vierhout ME. Trocar-guided mesh compared with conventional vaginal repair in recurrent prolapse: a randomized controlled trial. Obstet Gynecol. 2011 Feb;117(2 Pt 1):242-50.
- Altman D, Väyrynen T, Engh ME, Axelsen S, Falconer C; Nordic Transvaginal Mesh Group. Anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse. N Engl J Med. 2011 May 12;364(19):1826-36

The rates and severity of adverse events reported in the Prolift+M™ study are presented in Table 3, providing 29 months follow up post-surgery. Up to 29 month follow up following surgery, 96 adverse events were reported in 58 subjects (47.9%). Overall, the majority of events (66.7%) were considered to be mild in severity, with 27.1% and 6.2% considered to be moderate and severe, respectively.

Table 3: Cumulative rate and severity of adverse events following Prolift+M repair:

N=128	0-3 months	0-12 months	0-24 months	0-36 months
Number of patients reporting at least one AE	45 (35.2%)	69 (53.9%)	80 (62.5%)	84 (65.6%)
Total number of AEs	68	109	128	138
Mild	52 (76.5%)	83 (76.1%)	101 (78.9%)	109 (79.0%)
Moderate	12 (17.6%)	20 (18.3%)	21 (16.4%)	21 (15.2%)
Severe	4 (5.9%)	6 (5.5%)	6 (4.7%)	8 (5.8%)

Adverse events were categorized using the following definitions:

-Mild: Awareness of a sign or symptom that does not interfere with the subject's usual activity or is transient, resolved without treatment and with no sequelae

-Moderate: Interferes with the subject's usual activity

-Severe: Incapacitating with inability to work or perform usual activities

0-36months includes any AEs reported after 36 months

Table 4 summarizes the mesh-exposure data according to severity. The overall incidence of mesh exposure to 36 months was 14.8%, with the majority of mesh exposures occurring in the first 12 months following surgery, and with the exception of two exposures, all were considered to be mild in nature.

Table 4: Mesh exposure rate and severity of incidence over time (days)

Type of intervention for mesh exposure	N patients experiencing (n=128)	Number of new events at each time point**			
		6 months	12 months	24 months	36 months
None	1 (0.8%)	1	0	0	0
Medical[#]	3 (2.4%)	0	0	1	2
Minor / outpatient surgery*	10 (8.6%)	5	4	0	2
Inpatient surgery	4 (3.1%)	3	1	0	0
Unknown^	1 (0.8%)	0	1	0	0
Overall	19 (14.8%)	9	6	1	4

[#] All patients were treated with topical oestrogen
^ Pt 24013; patient withdrew consent prior to intervention so unknown
*Not possible to differentiate between intra-office and outpatient surgery
**Some patients had more than one event over time

The quality of life, including sexual function results, using validated instruments (PFDI-20, PFIQ-7, PGI-C and PISQ-12) for women following Prolift +M mesh repair through to 36 months are reported in Table 5. Validated instruments were utilized to assess the quality of life specific to the condition of prolapse. All of the changes observed were improvements compared to baseline, were statistically significant ($p<0.01$), and sustained over time.

Table 5: Quality of Life Data for patients treated with PROLIFT +M™ device

	All (n=127)				
	Baseline	3 months	12 months	24 months	36 months
PFDI-20	98.9 (52.0)	31.5 (26.4)*	25.9 (28.0)*	28.8 (29.2)*	28.0 (33.5)*
POPDI-6	41.4 (21.9)	5.9 (8.2)*	6.4 (9.9)*	7.2 (10.5)*	7.2 (11.4)*
CRADI-8	21.6 (17.0)	11.6 (12.3)*	10.6 (13.1)*	11.6 (14.4)*	11.1 (14.0)*
UDI-6	35.7 (25.0)	13.9 (17.1)*	9.1 (13.5)*	10.1 (13.4)*	9.6 (13.8)*
PFIQ-7	74.5 (70.5)	17.8 (36.6)*	9.5 (23.4)*	12.5 (30.3)*	9.5 (24.1)*
POPIQ-7	24.8 (27.7)	3.8 (12.0)*	1.9 (9.4)*	2.7 (9.8)*	2.2 (7.8)*
CRAIQ-7	18.4 (24.6)	4.8 (13.5)*	3.2 (10.0)*	4.0 (10.7)*	2.5 (7.5)*
UIQ-7	31.3 (27.6)	9.2 (16.7)*	5.3 (13.3)*	5.8 (13.9)*	4.8 (11.1)*
PISQ-12~	33.4 (7.8)	38.9 (4.9)*	39.3 (4.1)*	39.1 (4.5)*	39.8 (4.2)*
PGI-C					
Much better	-	95 (84.8%)	103 (86.6%)	99 (88.4%)	88 (89.8%)
A little better	-	11 (9.8%)	11 (9.2%)	8 (7.1%)	7 (7.1%)
About the same	-	3 (2.7%)	3 (2.5%)	4 (3.6%)	3 (3.1%)
A little worse	-	3 (2.7%)	1 (0.8%)	1 (0.9%)	-
Much worse	-	-	1 (0.8%)	-	-

Data presented as mean (standard deviation) or n (%). PFDI-20 and PFIQ-7 scores range from 0 (best score) to 300 (worst score); POPDI, CRADI, UID, POPIQ, CRAIQ, UIQ scores range from 0 (best score) to 100 (worst score); PISQ-12 scores range from 0 (worst score) to 48 (best score); ~denotes change in n numbers for PISQ-12 as this was only collected for patients who were sexually active (n=60).*$p<0.001$ compared to baseline.

Table 6:

Review of reported complaints to the company (Launch to August 2012)

Prolift+M	2008	2009	2010	2011	2012	Total Events
Erosion - Urinary Tract	0	0	0	18	103	121
Post-Operative Complication	26	55	8	7	4	100
Recurrence - Other	0	29	7	0	0	36
Exposure - Vagina	4	17	8	4	1	34
Infection	8	5	1	1	2	17
Label/IFU - Other	0	3	0	4	0	7
Other	0	1	0	3	3	7
Intra-Operative Complication	2	2	2	0	0	6
Post-Operative Incontinence	0	4	1	0	0	5
Urinary Tract Perforation/Tissue Damage	1	3	0	1	0	5
Pain	0	0	1	2	1	4
Colon/Rectum Perforation/Tissue Damage	0	1	1	0	0	2
Blood Loss - Other	0	2	0	0	0	2
Unintended Tissue Reaction	0	0	0	2	0	2
Dyspareunia	0	0	2	0	0	2
Label/Ifu Information Insufficient	0	2	0	0	0	2
Missing Component	0	0	1	0	1	2
Separation - Cannula Tip	0	0	0	1	0	1
Dislikes Packaging/Labeling	0	0	1	0	0	1
Open Seal	0	0	0	1	0	1
Blood Loss - Hematoma	0	0	0	1	0	1
Separation - Cannula Hub	0	0	1	0	0	1
Missing Component	0	0	0	1	0	1
Tip Configuration - Guide Needle	0	0	0	1	0	1
Adhesion Formation - Other	0	0	0	1	0	1
Organ Perforation/Tissue Damage - Other	1	0	0	0	0	1
Product Mix	0	1	0	0	0	1
Nonfunctional - Guide Needle	0	1	0	0	0	1
Total Events	42	126	34	48	115	365
Demand	-	13,457	19,677	19,767	9,662	62,563
Rate (per 10,000)	-	93.63	17.28	24.28	119.02	58.34

Table 7: MAUDE Review

A search of the Manufacturer and User Facility Device Experience (MAUDE) Database maintained by the U. S. Food and Drug Administration on Prosima from January 2007 through September 2012. 201 reports were directly related to complications related to the PROLIFT +M™ device (6 were double reports and 2 were not related to Prolift+M™). The search is summarized in the following table; no adverse events were detected that were not covered by the risk management diligence performed by Ethicon on the Prolift +M™ Pelvic Floor repair system:

Mesh exposure related to pain/ dyspareunia/ formation of scar tissue and one or multiple surgical procedures to revise	103*
Mesh exposure – surgical excision	17
Mesh exposure – Medical/no treatment	15
Mesh erosion into bladder	1
Mesh contraction – no treatment	2
Mesh contraction – pain – surgical revision	1
Dyspareunia (isolated) – no treatment	2
Peroperative Bladder Injury - uncomplicated	1
Peroperative Bladder Injury – mesh implantation aborted	1
Peroperative Bladder Injury – requiring ureteric stenting	2
Ureteric injury – bilateral – procedure abandoned	1
Post-op infection – Antibiotic R/ and mesh removal	2
Post-op infection – Antibiotic R/	7
Urinary tract infection	9
Peroperative Rectal Injury - uncomplicated	1
Bowel perforation- sepsis- death	1
Stress urinary incontinence	10
Urinary retention	2
“pain”	2
Sciatic pain – transient (3 months)	1
DVT – thrombectomy - resolved	1
Sponge left behind – revision – DVT –Pulmonary embolus - death	1
Pulmonary embolism – resolved	1
Recurrence of Prolapse	7
Bleeding postoperatively requiring reintervention	1
Undisclosed injuries	1
Total No of Complications	**193**

** 84 in 2012 related to litigation*

Table 8: To be able to put the benefit-risk profile related to Ethicon Inc.'s mesh based POP repair solutions in perspective, it is essential to recognize that *all* procedures to treat pelvic organ prolapse can be associated with similar complications. A meta-analysis by Diwadkar et al. demonstrated that traditional (native tissue) vaginal repairs, vaginal mesh repairs and sacrocolpopexy all have their own inherent risks that differ in number and severity; however, they all have similar total complication rates. (Note: Some of the publications involved in this meta-analysis relate to non-Ethicon Inc. mesh products.)

Table 8: Complication rate meta-analysis comparing traditional vaginal (native tissue) repairs with sacral colpopexy mesh repairs and transvaginal mesh kit repairs:

	Traditional vaginal repair	Sacral colpopexy	Mesh kits
Number of studies	48	52	24
Total Complication rate	15.3	17.1	14.5
Mesh exposure/ infection	0.5	2.2	5.8
Cystotomy	0.4	1.0	0.7
Ureteral injury	0.3	0.2	0.1
Bowel injury	0.4	0.5	0.3
Bleeding complication	2.8	1.6	1.1
Wound complications	0.5	1.5	0.2
PE / DVT	0.1	0.3	0
Dyspareunia	1.5	1.5	2.2
Total reoperation rate	5.8	7.1	8.5
Reoperation for prolapse recurrence	3.9	2.3	1.3
Total reoperation rate	5.8	7.1	8.5
Reoperation for prolapse recurrence	3.9	2.3	1.3

F. RISK / BENEFIT ANALYSIS:

The summary of the literature confirmed the safety and effectiveness of the Prolift+M™ procedure.
In a similar fashion, the technique used for the Prolift+M™ procedure has been used effectively and safely in the treatment of pelvic floor prolapse in vaginal mesh application in a procedure called the Prolift™ Pelvic Floor Repair System, which uses a different type of mesh.

Harms/Hazards Summary Table

The Harms/Hazards Table was created via procedural process mapping, and Application FMEA and Design FMEA. Internal and external sources (company sponsored trial data, complaint review and data from the literature) were utilized to create the Harms/Hazards Table.

Harm Definitions for Harm Categories in PR-000564	**Hazards**	**Severity Category**	**Frequency of Harm**	**Harm Risk Level**
Adhesions	Not applicable	S5	F0	Clear
		S4	F0	Clear
		S3	F0	Clear
		S2	F0	Clear
		S1	F0	Clear
Blood Borne Pathogen Transmission	No Hazards identified			Clear
		S5	F0	Clear
		S4	F0	Clear
		S3	F0	Clear
		S2	F0	Clear
		S1	F0	Clear
Blood Loss	-Device abraids small blood vessels -Hematoma -Inadvertent vascular injury inserter/dissection -Vaginal tearing	S5	F1	Yellow
		S4	F1	Yellow
		S3	F5	Yellow
		S2	F5	Yellow
		S1	F5	Green
Delayed Wound Healing	-Sutures did not re-approximate vaginal epithelium -Interference by foreign body	S5	F0	Clear
		S4	F0	Clear
		S3	F5	Yellow
		S2	F5	Yellow
		S1	F5	Green
Extended Surgery	-Unable to position mesh in dissected field - Physician supplements procedure with additional fixation points (sutures) -Illegible labeling -Damaged packaging -Puncturing balloon VSD -Periop complication	S5	F0	Clear
		S4	F0	Clear
		S3	F4	Yellow
		S2	F0	Clear
		S1	F5	Green
Electric Discharge (unintended)	N/A – Device does not contain electric components	S5	N/A	Clear
		S4	N/A	Clear
		S3	N/A	Clear
		S2	N/A	Clear
		S1	N/A	Clear

Harm	Hazards	Severity Category	Frequency of Harm	Harm Risk Level
Exposure	- Mesh exposure: vaginal, bladder, rectum, bowel, urinary tract (erosion) -Devascularized rectal/vaginal wall -Incorrect mesh placement (roping/ folding/…) -Too rigid device -Degraded mesh leading to bunching/wrinkling in mesh -Expired and/or contaminated product used -Incorrect dissection technique	S5	F0	Clear
		S4	F4	Red
		S3	F5	Yellow
		S2	F5	Yellow
		S1	F5	Green
Failure of Treatment	-Product not effective/inadequate support -Wound healing impaired -Tissue quality -Overcorrection (De novo stress incontinence) -Voiding difficulty -Inadequate dissection -Improper mesh placement	S5	F0	Clear
		S4	F0	Clear
		S3	F5	Yellow
		S2	F0	Clear
		S1	F0	Clear
Fistula Formation	-Ureter perforation resulting in urinoma -Vaginal tearing leading to vesico-vaginal or recto-vaginal fistula -Failure of injured sites to heal properly -Sinus tract that allows urine or stool to track along suture into vagina. -Mesh material ropes when setting appropriate tension -Insufficient tissue integration	S5	F0	Clear
		S4	F3	Yellow
		S3	F4	Yellow
		S2	F0	Clear
		S1	F0	Clear
Infection	-Mesh placed in patients with active or latent infection -Bowel Perforation -Inadvertent opening of a hollow viscus (enterotomy, cystotomy, ureterotomy) -Inadvertent colon/Ureteral injury -Contaminated product used -Osteitis -Insufficient tissue integration -Compromised sterile barrier -Sepsis -Device reuse	S5	F1	Yellow
		S4	F3	Yellow
		S3	F5	Yellow
		S2	F0	Clear
		S1	F0	Clear
Inflammatory or other Unintended Tissue Reaction	-Severe Inflammatory response (device not biocompatible) -Scar-mesh contracture	S5	F0	Clear
		S4	F0	Clear
		S3	F4	Yellow
		S2	F0	Clear
		S1	F0	Clear

Harm	Hazards	Severity Category	Frequency of Harm	Harm Risk Level
Internal Organ Damage	-Excessive dissection -Bowel/bladder/Urethral/Ureteral injury -Organ injury during trocar placement -Vaginal Tearing -Inadvertent enterotomy (opening of bowel) -Inadvertent cystotomy -Inadvertent colon injury -Incarceration of bowels -Ureter kinking	S5	F0	Clear
		S4	F4	Red
		S3	F5	Yellow
		S2	F0	Clear
		S1	F5	Green
Nerve Damage / Pain	-Chronic Pain -Femoral Nerve Palsy -Peroneal Nerve Palsy -Chronic inflammation around mesh and bladder wall and/or rectal wall -Inadvertent nerve damage -Dyspareunia -Injury to autonomic nerves -Increased scar Formation	S5	F0	Clear
		S4	F4	Red
		S3	F5	Yellow
		S2	F5	Yellow
		S1	F0	Clear
Skeletal / Cartilage Damage	Osteitis	S5	F0	Clear
		S4	F0	Clear
		S3	F1	Green
		S2	F0	Clear
		S1	F0	Clear
Soft Tissue Damage	-Mesh exposure: vaginal, bladder,rectum,bowel,UT -Devascularized rectal/vaginal wall -Mesh banding (roping) -Too rigid device -Improper wound closure -Degraded mesh leading to bunching/wrinkling in mesh -Expired and/or contaminated product used	S5	F0	Clear
		S4	F4	Red
		S3	F5	Yellow
		S2	F5	Yellow
		S1	F0	Clear
Thromboembolic Event	-Deep Vein Thrombosis/Pulmonary Embolus	S5	F3	Red
		S4	F4	Red
		S3	F4	Yellow
		S2	F0	Clear
		S1	F0	Clear

Severity Category Definitions

Severity Category Table

PR551-006 Designation	Severity Category	Definition for use in Ethicon Risk Management
Serious Injury (Reportable)	S5	Acutely life-threatening or fatal
	S4	Permanent or long term impairment of body function or Permanent or long term damage to a body structure.
	S3	Necessitates intrusive medical or surgical intervention.
Non-Reportable	S2	Injury is temporary or reversible (without intrusive medical intervention)
	S1	Limited (inconvenience or temporary discomfort, transient, or complaints).
	S0	No adverse health consequences. Not a Harm.

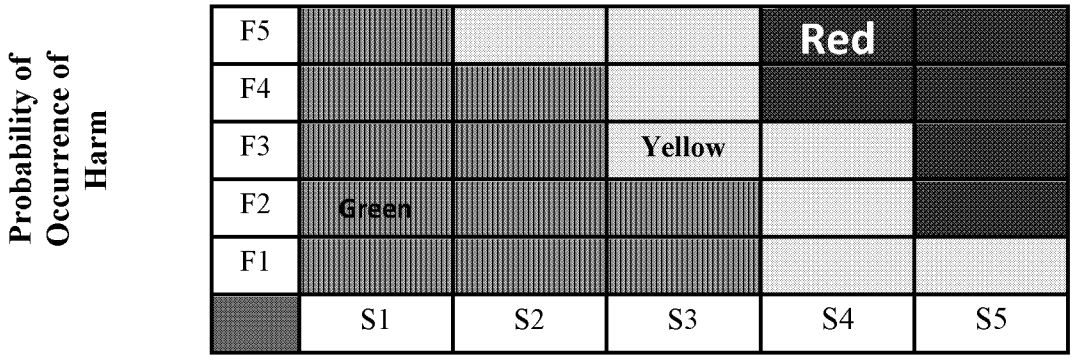
Frequency of Harm

Harm Frequency Estimation Table

Ranking of Frequency (F)	Variable Description*	
	Frequency	Percentage
F5	> 1/100	> 1%
F4	1/100 - 1/1000	0.1% - 1%
F3	1/1000 - 1/5000	0.02% - 0.1%
F2	1/5000 - 1/10,000	0.01% - 0.02%
F1	1/100,000 - 1/10,000	0.001% - 0.01%
F0	< 1/100,000	< 0.001%

Harm Risk Level

Risk Summary Table



High risk categories

High risk categories were identified for: (reference: RMR-0000029)

1. Exposure: Exposure was reported upon in 110 studies in a meta-analysis, entitled "Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review" by Abed et al. yielding an average incidence of 10.3% (IUJ 2011). Similarly, the prospective study on Prolift+M™ reported an 10.2% exposure rate during the first year. Table 4 above summarizes the mesh-exposure data according to severity. Of note is that only 4 of the 15 incidences of mesh exposure required an inpatient surgical intervention during the first year. Five more exposures were discovered between the 12 and 36 months follow up period. None of these required inpatient surgical intervention.
   A review article on Prolift™ (not Prolift+M) stated that 0.6% of patients after Prolift insertion required excision for severe mesh-related complications and 11% for minor complications (Tijdink et al. IUJ 2011). This incidence in combination with the prospective Prolift+M data justify the estimated frequency of permanent or long term impairment to be 1/100 to 1/1000.

2. Internal organ damage may occur. Bowel and bladder injuries were encountered in 0.3% and 1.9% respectively in a Prolift analysis of 3194 patients. This corresponds to the 0 and 2.3% for bowel and bladder respectively reported in the prospective Prolift+M trial (Tabel1). This justifies the frequency assigned to this complication of 1%. However, internal organ damage in vaginal surgery should not be considered life-threatening: they may require (additional) surgery and/or antibiotic treatment, but the majority is easily manageable during the index surgery. Only if they lead to sepsis as described above could it become fatal, this has not been reported to date in the literature nor in the MAUDE or ETHICON's complaint database.

3. Nerve damage and/or pain: The prospective Prolift+M trial described pelvic pain (pelvic discomfort and vagina pain) in 6.3%. In 3.1% of patients de novo dyspareunia was identified over a 36 months period. In a review of the Prolift literature 9 studies reported on the issue of dyspareunia and on average was reported in 12.7%. Dyspareunia was described in 70 studies for a rate of 9.1% in a meta-analysis entitled "Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review." by Abed et al. (IUJ 2011). These dyspareunia rates correspond to rates observed in traditional pelvic organ prolapse repairs (Lowman et al, AJOG 2008). The injuries are often mild and transient. In rare instances will they lead to permanent damage. A review article on Prolift™ states that 0.6% of patients require excision for severe mesh-related complications and 11% for minor complications (Tijdink IUJ 2011). The data in the literature and from the 36 month prospective Prolift+M study justify the estimated frequency of permanent damage to be maximally 1/100 to 1/1000.

4. Soft tissue damage: These rates are explained under the harm of exposure.

5. Deep venous thrombosis (DVT) is the most common non-surgical complication after major pelvic (gynecologic) surgery and is potentially fatal when it leads to pulmonary thrombo-embolism. The rates of DVT in patients undergoing major gynecologic surgery in the absence of DVT prophylaxis are reported in various reviews as 6% to 29%. With the use of heparin prophylaxis these rates have been significantly reduced. A rate between 0.1% and 1% for each invidual throboembolic complication therefore seems a correct estimate of its frequency in these elective benign procedures. (Source: Davis J.D.: Prevention, diagnosis, and treatment of venous thromboembolic complications of gynecologic surgery. Am J Obstet Gynecol 2001; 184: 759-75.)

Risk benefit conclusion:

The PROLIFT +M™ Pelvic Floor Repair System is a mesh kit used to treat pelvic organ prolapse. Review by medical affairs has confirmed that the evidence demonstrates an acceptable benefit-risk profile for these products when placed in appropriately selected patients by experienced surgeons. Adverse events associated with transvaginal mesh kits are well characterized and are manageable in the majority of cases. No new adverse events have been identified since the product's initial launch.

The anticipated medical benefits outweigh the Overall or Individual Residual Risk(s) associated with this device. The Prolift +M™'s proven beneficial impact on anatomical and functional outcomes in combination with its comparable overall complication rates in relation to traditional pelvic organ prolapse repairs (including sacrospinous ligament fixations and abdominal sacrocolpopexies) and the manageability of the mesh specific complications support the Prolift+M™ Pelvic Floor Repair System as a state of the art treatment option for certain patients suffering from pelvic organ prolapse.

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G. APPENDIX: INSTRUCTIONS FOR USE